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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--------------------------|-------------|----------------------|---------------------|------------------|
| 09/919,298 | 07/31/2001 | Joseph Edward Zahner | 16850-8184 | 2484 |
| 32809 | 7590 | 10/03/2003 | EXAMINER | |
| NUCLEUS REMODELING, INC. | | | WOITACH, JOSEPH T | |
| 3646 DOVER PLACE | | | ART UNIT | |
| ST. LOUIS, MO 63116 | | | PAPER NUMBER | |
| | | | 1632 | |

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/919,298

Applicant(s)

ZAHNER ET AL.

Examiner

Joseph T. Woitach

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 September 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: The term "Oct-4" is a new embodiment not previously searched nor considered.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:


Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1,3-5,8,21 and 22.

Claim(s) withdrawn from consideration: 23-33.

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
10. ☐ Other: _____


DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
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Continuation of 5. does NOT place the application in condition for allowance because: In addition it is noted that the editing marks for the addition and recitation of 'Oct-4 in claim 1 was not made in applicants' amendment. While the claim appears to be clear and complete, claim amendments filed under 37 CFR 1.116 should clearly indicate all changes made to the claims. Not providing amendments in the required format raises new issues of formal matters. With respect to Applicants' arguments and declaration filed under 37 CFR 1.132, they have been fully considered but not found persuasive. With respect to Applicants' arguments Examiner would agree in general that the treatment with one or each of the three types of reagents would affect nuclear remodelling resulting in changes in gene expression, however in question is what the resulting 'reprogrammed' cell represents. The specific results in the disclosure and the declaration provide evidence that gene expression changes and that multiple genes representing multiple cell type lineages are expressed after treatment but there is an insufficient correlation with the change in gene expression to conclude that the resulting cell is a pluripotent stem cell. For example, transformed cells are known in the art to regain expression of telomerase and some of the teratoma tumor type cells have been demonstrated to express Oct-4. Similarly, there are transformed cell lines which are known to express SSEA-1. Additionally, the results set forth in experiments to demonstrate differentiation by adding retinoic acid to the treated cells provides evidence the cells can be further affected, however whether the changes reflect differentiation of a stem cell have not been firmly established. Further, it is unclear whether the proposed amendment for the capability of the resulting cell to express a 'neurofilament, cardiac actin and alpha antitrypsin' fairly represents a pluripotent stem cell. Examiner does not contest the specific results which have been reduced to practice in the instant disclosure and the declaration filed with the after final amendment, rather at issue is whether these results represent the breadth of the claims for making pluripotent stem cells from any organism and if the specific results provide a nexus for other cell types or the use of other agents in the re-programming process.